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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/631,152	08/02/2000	Jon A. Wolff	Mirus.017.01	8109

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Mark K. Johnson
P. O. Box 510644
New Berlin, WI 53131-0644

EXAMINER	
SULLIVAN, DANIEL M	
ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 03/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/631,152	WOLFF ET AL.	
	Examiner	Art Unit	
	Daniel M Sullivan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-5,7-16 and 18-33* is/are pending in the application.

4a) Of the above claim(s) *18-33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-5 and 7-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 August 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *22 December 2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the Office Action mailed 26 August 2003 has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 22 December 2003 has been entered.

Claims 18-33 had been withdrawn from consideration and claims 1 and 3-17 were considered in the 26 August Office Action. Claims 6 and 17 were canceled and claims 1, 5, 7 and 14 were amended in the 22 December Paper.

Claims 1, 3-5, 7-16 and 18-33 are pending and claims 1, 3-5 and 7-16 are under consideration.

Response to Amendment

Rejection of claims 6 and 17 is rendered moot by cancellation of the claims.

Claim Objections

Objection to claim 1 is withdrawn.

Claim Rejections - 35 USC § 112

Claims 1, 3-5 and 7-16 stand rejected under 35 U.S.C. 112, first paragraph, as lacking adequate written description for reasons of record. The amended claims still encompass subject

matter indicated as lacking adequate written description and the remarks contain no statement rebutting the *prima facie* case.

Claims 1, 3-5 and 7-16 stand rejected under 35 U.S.C. 112, first paragraph, as lacking enablement for the full scope of the claimed subject matter for reasons of record and herein below in the response to arguments.

Claims 14-16 stand rejected under 35 U.S.C. 112, second paragraph, as indefinite in using the indefinite article to refer to the base claim. The amendment does not address these grounds for rejection, originally set forth in the 16 December 2002 Office Action; therefore, the claims stand rejected for reasons of record.

Rejection of claims 1, 3-5 and 7-16 under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation of "nucleic acid modifying agent" and in lacking antecedent basis for "the compound" is withdrawn.

Response to Arguments

Claim Rejections - 35 USC § 112

Claims 1, 3-5 and 7-16 were rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a process for nucleic acid delivery to a cell *in vitro*, comprising: (a) preparing a nucleic acid molecule having an expressible sequence; (b) attaching a compound to the nucleic acid molecule within the expressible sequence, utilizing a modifying

chemical attachment; and, (c) delivering the nucleic acid to a cell where the expressible sequence is expressed, wherein said compound is selected from the group consisting of rhodamine, DNP, digoxin, biotin, and the peptide nuclear localization sequence CPKKKRKVEDG, does not reasonably provide enablement for a process for nucleic acid delivery to a cell *in vivo* or a process for nucleic acid delivery to a cell *in vitro* wherein the compound is *any* compound or nuclear localizing signal, ligand that binds a receptor, releasing signal, enhanced immune response molecule, antigen, antibody, hapten, membrane active compound, peptide, polymer, polyion and fluorescent compound.

In reply to the arguments of record, Applicant states, "while therapeutic effects may be a derivative of gene therapy, the definition of the terminology 'gene therapy' is not limited to that single result. The National Cancer Institute defines gene therapy as 'treatment that alters a gene (the basic units of heredity found in all cells in the body)'". Applicant argues that the specification does not define gene therapy to such that it is limited to providing a therapeutic result and urges that delivery of genes for research purposes is within the definition of gene therapy.

These arguments have been fully considered but are not deemed persuasive. First, Applicant bases the arguments on a statement alleged to be the National Cancer Institute definition of gene therapy. However, it is impossible to ascertain the true meaning of the cited statement because applicant does not identify its source, except for broadly attributing the statement to the National Cancer Institute. In the absence of any specific context, it is unclear what is actually meant by the sentence fragment quoted by Applicant. Furthermore, Applicant is reminded that Office personnel must rely on the applicant's disclosure to properly determine the

meaning of terms used in the claims. *Markman v. Westview Instruments*, 52 F.3d 967, 980, 34 USPQ2d 1321, 1330 (Fed. Cir.) (*en banc*), aff 'd, U.S. , 116 S. Ct. 1384 (1996). Where an explicit definition is provided by the applicant for a term, that definition will control interpretation of the term as it is used in the claim. *Toro Co. v. White Consolidated Industries Inc.,* 199 F.3d 1295, 1301, 53 USPQ2d 1065, 1069 (Fed. Cir. 1999). Page 2 of the specification states, "[d]elivery of functional polynucleotides or other genetic material for therapeutic purposes is gene therapy" (lines 23-24). For the purpose of examining the instant claims, this is the controlling definition of gene therapy regardless of the National Cancer Institute definition.

Next, it should be made clear that, the enabling specification must teach those skilled in the art to make and use the full scope of the claimed invention without undue experimentation. "Although not explicitly stated in section 112, to be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.' *Vaeck*, 947 F.2d at 495, 20 USPQ2d at 1444; *Wands*, 858 F.2d at 736-37, 8 USPQ2d at 1404; *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (the first paragraph of section 112 requires that the scope of protection sought in a claim bear a reasonable correlation to the scope of enablement provided by the specification)." *In re Wright* (CAFC) 27 USPQ2d 1510 at 1513.

Thus, even if the claimed method were to encompass delivery of genes for research purposes, there is nothing in the claims that excludes gene therapy from the claimed subject matter. Given that the teachings set forth in the specification with regard to how to use the claimed method are predominantly focused on gene therapy applications, gene therapy is clearly

within the scope of the claims and therefore must be enabled for the skilled artisan to practice the full scope of the claimed method.

In the paragraph bridging pages 4-5, Applicant cites several articles as evidence that nucleic acid modification agents can be used for research and development. However, to the extent that the cited art teaches methods similar to that of the instant claims, only one teaches *in vivo* gene transfer and expression, and none suggests enablement for a method encompassing delivery of a nucleic acid for therapeutic effect as encompassed by the instant claims.

Applicant takes issue with the statement in the previous Office Action that, "delivering a nucleic acid to a cell is not in and of itself a patentable utility." Applicant urges that a vast body of research is focused solely on methods to deliver a nucleic acid to a cell and that the present invention relates to a process of modifying a gene such that the gene can be efficiently expressed in a cell. First, it should be made clear that the statement cited by Applicant was made in response to Applicant's contention that, "[t]he nature of the expressible nucleic acid and purpose for which it is delivered does not affect the claimed process..." (first full paragraph on page 8). When viewed in context, it is clear that the Examiner is merely explaining why the claims have been construed to encompass gene therapy. That is, because the claims recite only "a process for delivery of a modified expressible nucleic acid...", which does not convey or limit the claim to any particular useful outcome, the scope of the claim must be construed based on the teachings set forth in the specification. As therapy is clearly a focus of the teachings with regard to how the claimed invention will be used, therapeutic application is within the scope of the claims and must be enabled.

Next, Applicant cites working examples demonstrating an augmented antibody response against a reporter gene and improved *in vivo* reporter gene expression. However, the claims are not limited to a method of obtaining an augmented antibody response or improving expression of a reporter gene. Applicant seems to be arguing that the claims are enabled in spite of the lack of enablement for gene therapy because research applications are within the scope of the claims. However, the claims are clearly not limited to research application and as pointed out in the previous Office Action: in the paragraph bridging pages 2-3, the specification teaches gene therapy by expression of a whole or partial protein or antisense; on page 3, the specification contemplates gene replacement therapy of Duchenne muscular dystrophy, as well as treatment of neurodegenerative disorders, cancer, heart disease and infections using the claimed invention; and the specification further teaches expression of therapeutic genes such as erythropoietin, FGF and VEGF. Although the claims are not explicitly limited to gene therapy, it is clear from the disclosure that the intended use for the claimed method is gene therapy, and that the method is to be used for gene therapy of extremely complicated diseases such as muscular dystrophy, neurodegenerative disorders, cancer and heart disease. As there is nothing in the claims that would exclude this subject matter, the claims are construed to encompass methods of gene therapy and for reasons of record lack enablement therefor.

Finally, the scope of the compound of the claims is the same as in the previous claim sets and Applicant's remarks contain no rebuttal of the grounds for lack of enablement for the method wherein the compound other than rhodamine, DNP, digoxin, biotin, or the peptide nuclear localization sequence CPKKKRKVEDG. Therefore, the claims stand rejected as lacking enablement for the method practiced with the full scope of the encompassed compounds.

Applicant's arguments have been fully considered but are not deemed persuasive either individually or as a whole. Therefore, the claims stand rejected under 35 U.S.C. §112, first paragraph, as lacking enablement for the full scope of the claimed subject matter.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 571-272-0779. The examiner can normally be reached on Monday through Friday 8-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

DMS

Anne-Marie Falk

ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER